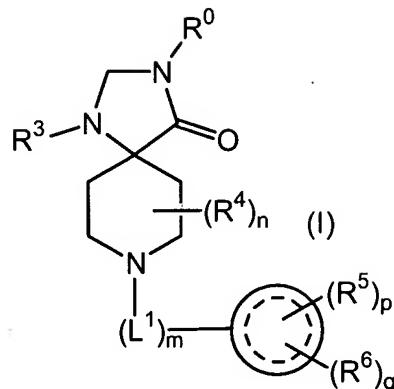


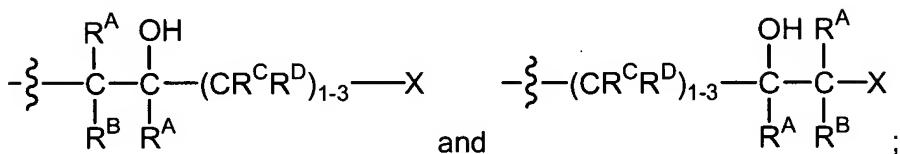
What is claimed is:

1. A compound of the formula (I)



5 wherein

R^0 is selected from the group consisting of



each R^A and R^B is independently selected from the group consisting of hydrogen and C_{1-4} alkyl;

10 each R^C and R^D is independently selected from the group consisting of hydrogen, hydroxy, carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, nitro, cyano, $N(R^E)_2$, aryl, ar C_{1-4} alkyl, heteroaryl or heterocycloalkyl; wherein the aryl, ar C_{1-4} alkyl, heteroaryl or heterocycloalkyl substituent is optionally substituted with one or more substituents independently selected from hydroxy, carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, nitro, cyano or $N(R^E)_2$;

15 each R^E is independently selected from the group consisting of hydrogen and C_{1-4} alkyl;

20 X is selected from the group consisting of $-NR^1R^2$, $-C(O)-NR^1R^2$, $-NR^1-C(O)-R^2$, $-OR^1$, $-SR^1$, $-SOR^1$, $-SO_2R^1$, $-S-(C_{2-4}\text{alkyl})-NR^1R^2$, $-S-(C_{2-4}\text{alkyl})-C(O)O-C(CH_3)_3$, $-SO-(C_{1-4}\text{alkyl})-NR^1R^2$ and $-SO_2-(C_{1-4}\text{alkyl})-NR^1R^2$; wherein the alkyl portion of the $-S-(C_{2-4}\text{alkyl})-NR^1R^2$, $-SO-(C_{1-4}\text{alkyl})-NR^1R^2$ or $-SO_2-(C_{1-4}\text{alkyl})-NR^1R^2$ group is optionally substituted with one or more substituents independently selected from carboxy, hydroxy, hydroxy C_{1-4} alkyl, C_{1-4} alkyl, C_{1-4} alkoxycarbonyl or $-CONR^1R^2$;

each R¹ and R² is independently selected from the group consisting of hydrogen, C₁₋₈alkyl, C₁₋₈alkoxy, C₁₋₈alkoxycarbonyl, cycloalkyl, cycloalkyl-C₁₋₄alkyl, partially unsaturated carbocyclyl, partially unsaturated carbocyclyl-C₁₋₄alkyl, aryl, arC₁₋₄alkyl, arC₁₋₄alkoxy, heteroaryl, heteroaryl-C₁₋₄alkyl,

5 heterocycloalkyl, heterocycloalkyl-C₁₋₄alkyl, -C(O)-C₁₋₆alkyl, -C(O)-aryl, -C(O)-arC₁₋₄alkyl, -C(O)-heteroaryl, -C(O)-heterocycloalkyl, -C(O)O-cycloalkyl and -C(O)O-aryl, -C(O)O-arC₁₋₄alkyl, -C(O)O-(partially unsaturated carbocyclyl), -C(O)O-heteroaryl, -C(O)O-heterocycloalkyl; wherein the C₁₋₈alkyl, cycloalkyl, partially unsaturated carbocyclyl, aryl, arC₁₋₈alkyl, heteroaryl or heterocycloalkyl

10 group, whether alone or part of a substituent group, is optionally substituted with one or more substituents independently selected from halogen, hydroxy, carboxy, C₁₋₄alkyl, C₁₋₄alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano, -C(O)-C₁₋₄alkyl, C₁₋₄alkoxycarbonyl, N(R^E)₂, N(R^E)₂-C₁₋₄alkyl, N(R^E)-C(O)C(CH₃)₃, -C₁₋₄alkyl-N(R^E)-C(O)O-C₁₋₄alkyl and -N(R^E)-C(O)O-C₁₋₄alkyl,

15 aryl, aryloxy, cycloalkyl, heteroaryl, aryl substituted heteroarylamino sulfonyl or C₁₋₆alkylthio;

alternatively when R¹ and R² are both bound to the same nitrogen atom, R¹ and R² are taken together with the nitrogen atom to which they are bound to form a heteroaryl or heterocycloalkyl group; wherein the heteroaryl or

20 heterocycloalkyl group is optionally substituted with one or more substituents independently selected from halogen, hydroxy, carboxy, C₁₋₄alkyl, hydroxy substituted C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkoxycarbonyl, trifluoromethyl, trifluoromethoxy, nitro, cyano, N(R^E)₂, aryl, arC₁₋₄alkyl, heteroaryl, heterocycloalkyl, di(C₁₋₆)alkylamino-carbonyl, C₁₋₄alkoxycarbonyl-N(R^E)- or

25 arylamino-C₁₋₄alkyl; wherein the aryl, arC₁₋₄alkyl, heteroaryl or heterocycloalkyl substituent is optionally further substituted with one or more substituents independently selected from halogen, hydroxy, carboxy, C₁₋₄alkyl, C₁₋₄alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano, N(R^E)₂, phenyl or substituted phenyl; wherein the substituents on the phenyl are one or more independently

30 selected from halogen, hydroxy, carboxy, C₁₋₄alkyl, C₁₋₄alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano or N(R^E)₂;

R³ is selected from the group consisting of aryl, arC₁₋₆alkyl and heteroaryl; wherein the aryl, arC₁₋₆alkyl or heteroaryl group is optionally

substituted with one or more substituents independently selected from halogen, hydroxy, carboxy, C₁₋₄alkyl, C₁₋₄alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano or N(R^E)₂;

n is an integer from 0 to 2;

5 R⁴ is selected from the group consisting of hydroxy, C₁₋₄alkyl and hydroxy substituted C₁₋₄alkyl;

m is an integer from 0 to 1;

L¹ is selected from the group consisting of C₁₋₆alkyl and C₃₋₆alkenyl; wherein the double bond of the C₃₋₆alkenyl group is at least one carbon atom

10 removed from the attachment point to the N atom; and wherein the C₁₋₆alkyl or C₃₋₆alkenyl group is optionally substituted with one to two substituents independently selected from hydroxy, fluoro, C₁₋₆alkyl, fluorinated C₁₋₆alkyl or C₁₋₆alkoxy;

 is selected from the group consisting of cycloalkyl, partially

15 unsaturated carbocyclyl, aryl, heteroaryl and heterocycloalkyl;

p is an integer from 0 to 5;

R⁵ is selected from the group consisting of hydroxy, carboxy, halogen, C₁₋₆alkyl, hydroxy substituted C₁₋₆alkyl, C₁₋₆alkoxy, nitro, cyano, NR¹R², trifluoromethyl, trifluoromethoxy, C₁₋₄alkoxycarbonyl, -SO-NR¹R², -SO₂-NR¹R² and -C(O)-NR¹R²;

20 q is an integer from 0 to 1;

R⁶ is selected from the group consisting of -(L²)₀₋₁-R⁷;

L² is selected from the group consisting of -C₁₋₆alkyl-, -C₂₋₄alkenyl-, -C₂₋₆alkynyl-, -O-, -S-, -NH-, -N(C₁₋₄alkyl)-, -C₁₋₆alkyl-O-, -C₁₋₆alkyl-S-, -O-C₁₋₆alkyl-, -S-C₁₋₆alkyl-, -O-C₂₋₆alkyl-O-, -S-C₂₋₆alkyl-S-, -SO₂-, -SO₂NH-, -SO₂N(C₁₋₄alkyl)-, -NH-SO₂-, -N(C₁₋₄alkyl)-SO₂-, -C(O)-O- and -O-C(O)-;

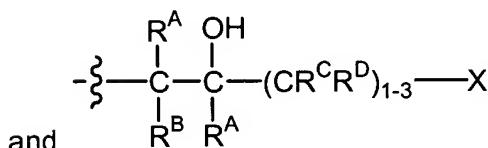
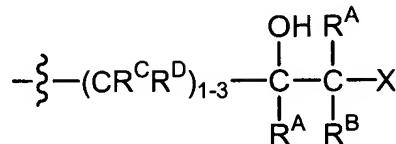
25 R⁷ is selected from the group consisting of aryl, partially unsaturated carbocyclyl, cycloalkyl, heteroaryl and heterocycloalkyl; wherein the aryl, partially unsaturated carbocyclyl, cycloalkyl, heteroaryl or heterocycloalkyl

30 group is optionally substituted with one or more substituents independently selected from hydroxy, carboxy, halogen, C₁₋₆alkyl, C₁₋₆alkoxy, nitro, cyano,

$N(R^E)_2$, trifluoromethyl, trifluoromethoxy, C_{1-4} alkoxycarbonyl, $-SO_2-N(R^E)_2$ and $-C(O)-N(R^E)_2$;

or a pharmaceutically acceptable salt thereof.

5 2. A compound as in Claim 1 wherein



each R^C and R^D is independently selected from hydrogen, C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy, carboxy or aryl; wherein the aryl is optionally substituted with one to two substituents independently selected from hydroxy, carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, nitro, cyano or $N(R^E)_2$;

10 X is selected from the group consisting of $-NR^1R^2$, $-C(O)-NR^1R^2$, $-NR^1-C(O)-R^2$, $-OR^1$, $-SR^1$, $-SO-R^1$, $-SO_2-R^1$, $-S-(C_{2-4}\text{alkyl})-NR^1R^2$, $-S-(C_{2-4}\text{alkyl})-NR^1-C(O)OC(CH_3)_3$, $-SO-(C_{1-4}\text{alkyl})-NR^1R^2$ and $-SO_2-(C_{1-4}\text{alkyl})-NR^1R^2$; wherein the 15 alkyl portion of the $-S-(C_{2-4}\text{alkyl})-NR^1R^2$, $-SO-(C_{1-4}\text{alkyl})-NR^1R^2$ or $-SO_2-(C_{1-4}\text{alkyl})-NR^1R^2$ group is optionally substituted with one to two substituents independently selected from C_{1-4} alkyl, hydroxy C_{1-4} alkyl, C_{1-4} alkoxycarbonyl or carboxy;

20 R^1 is selected from the group consisting of hydrogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, aryl, $arC_{1-4}\text{alkyl}$, $arC_{1-4}\text{alkyloxy}$, heteroaryl, heteroaryl-alkyl, heterocycloalkyl, heterocycloalkyl-alkyl, cycloalkyl-alkyl, $C(O)-C_{1-4}\text{alkyl}$ and $-C(O)-\text{heteroaryl}$;

25 wherein the $C_{1-4}\text{alkyl}$, aryl, $arC_{1-4}\text{alkyl}$, heteroaryl, heterocycloalkyl or cycloalkyl group, whether alone or part of a substituent group, is optionally substituted with one to three substituents independently selected from halogen, hydroxy, carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, $N(R^E)_2$, $N(R^E)_2-C_{1-4}\text{alkyl}$, $N(R^E)-C(O)OC(CH_3)_3$, nitro, trifluoromethyl, trifluoromethoxy, phenyl,

phenoxy, heteroaryl, cycloalkyl, 1-phenyl-pyrazol-2-yl-aminosulfonyl or C₁-alkylthio;

R² is selected from the group consisting of hydrogen, C₁₋₄alkyl, C₁₋₄alkoxy, cycloalkyl, cycloalkyl-C₁₋₄alkyl, aryl, arC₁₋₄alkyl, arC₁₋₄alkyloxy, partially unsaturated carbocyclyl, partially unsaturated carbocyclyl-C₁₋₄alkyl, heteroaryl, heteroaryl-C₁₋₄alkyl, heterocycloalkyl, heterocycloalkyl-C₁₋₄alkyl, -C(O)-C₁₋₄alkyl, -C(O)-aryl, -C(O)-arC₁₋₄alkyl, -C(O)-heteroaryl, -C(O)-heterocycloalkyl, -C(O)O-cycloalkyl and -C(OO)-C₁₋₄alkyl;

wherein the C₁₋₄alkyl, aryl, arC₁₋₄alkyl, partially unsaturated carbocyclyl, heteroaryl, heterocycloalkyl or cycloalkyl group, whether alone or part of a substituent group, is optionally substituted with one to three substituents independently selected from halogen, hydroxy, carboxy, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkoxycarbonyl, N(R^E)₂, N(R^E)₂-C₁₋₄alkyl, (CH₃)₃COC(O)-N(R^E)-C₁₋₄-alkyl, nitro, cyano, trifluoromethyl, trifluoromethoxy, phenyl, phenoxy, heteroaryl, cycloalkyl, 1-phenyl substituted heteroaryl-aminosulfonyl, -C(O)-C₁₋₄alkyl or C₁₋₄alkylthio;

alternatively when R¹ and R² are both bound to the same nitrogen atom, R¹ and R² are taken together with the nitrogen atom to which they are bound to form a heteroaryl or heterocycloalkyl group;

wherein the heteroaryl or heterocycloalkyl is optionally substituted with one to three substituents independently selected from halogen, hydroxy, carboxy, C₁₋₄alkyl, hydroxy substituted C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkoxycarbonyl, trifluoromethyl, trifluoromethoxy, nitro, cyano, N(R^E)₂, phenyl, arC₁₋₄alkyl, heterocycloalkyl, di(C₁₋₄alkyl)amino-carbonyl, C₁₋₄alkoxycarbonylamino or phenylamino-C₁₋₄alkyl;

wherein the phenyl or arC₁₋₄alkyl substituent on the heteroaryl or heterocycloalkyl group is optionally substituted with one or two substituents independently selected from halogen, hydroxy, carboxy, C₁₋₄alkyl, C₁₋₄alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano, N(R^E)₂ or substituted phenyl;

wherein the substituents on the phenyl are one to three independently selected from halogen;

R^3 is selected from the group consisting of aryl and arC₁₋₄alkyl; wherein the aryl or arC₁₋₄alkyl group is optionally substituted with one to three substituents independently selected from halogen, hydroxy, carboxy, C₁₋₄alkyl, C₁₋₄alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano or N(R^E)₂;

5 n is an integer from 0 to 1;

L^1 is C_{1-4} alkyl; wherein the C_{1-4} alkyl group is optionally substituted with one to two substituents independently selected from hydroxy, fluoro, C_{1-4} alkyl, fluorinated C_{1-4} alkyl or C_{1-4} alkoxy;

R^5 is selected from the group consisting of hydroxy, carboxy, halogen,

10 C₁₋₄alkyl, C₁₋₄alkoxy, nitro, cyano, N(R^E)₂, trifluoromethyl, trifluoromethoxy, C₁₋₄alkoxycarbonyl, -SO- N(R^E)₂, -SO₂- N(R^E)₂ and -C(O)- N(R^E)₂;

L^2 is selected from the group consisting of -C₁₋₄alkyl-, -O-, -S-, -N(R^E)-, -C(O)O- and -O-C(O)-;

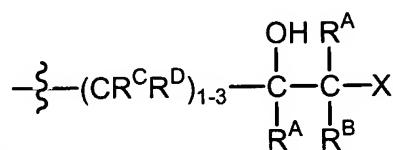
R^7 is selected from the group consisting of cycloalkyl, aryl, heteroaryl

15 and heterocycloalkyl; wherein the aryl, heteroaryl or heterocycloalkyl group is
optionally substituted with one to two substituents independently selected from
hydroxy, carboxy, halogen, C₁₋₄alkyl, C₁₋₄alkoxy, nitro, cyano, N(R^E)₂,
trifluoromethyl, trifluoromethoxy or C₁₋₄alkoxycarbonyl;

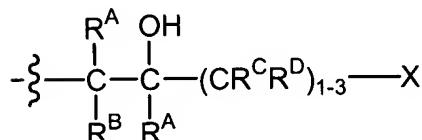
or a pharmaceutically acceptable salt thereof.

20

3. A compound as in Claim 2 wherein



R^0 is selected from the group consisting of



and $R^B R^A$

each R^A , R^B , R^C and R^D is hydrogen;

25 X is selected from the group consisting of -NR¹R², -OR¹, -SR¹, -S-(C₂-₄alkyl)-NR¹R² and -S-(C₂₋₄alkyl)-NR¹-C(O)O-C(CH₃)₃; wherein the alkyl portion of the -S-(C₂₋₄alkyl)-NR¹R² or -S-(C₁₋₄alkyl)-NR¹-C(O)O-C(CH₃)₃ group is optionally substituted with a carboxy or C₁₋₄alkoxycarbonyl group;

R^1 is selected from the group consisting of hydrogen, C_{1-4} alkyl, C_{1-4} alkoxycarbonyl, ar C_{1-4} alkyl and $C(O)-C_{1-4}$ alkyl;
 wherein the C_{1-4} alkyl or aryl group, whether alone or part of a substituent group, is optionally substituted with one to two substituents independently selected from carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, $N(R^E)_2$ or $N(R^E)-C(O)OC(CH_3)_3$;

R^2 is selected from the group consisting of hydrogen, C_{1-4} alkyl, C_{1-4} alkoxy, cycloalkyl, aryl, ar C_{1-4} alkyl, ar C_{1-4} alkyloxy, partially unsaturated carbocyclyl, partially unsaturated carbocyclyl- C_{1-4} alkyl, heteroaryl, heteroaryl- C_{1-4} alkyl, heterocycloalkyl, heterocycloalkyl- C_{1-4} alkyl, cycloalkyl- C_{1-4} alkyl, - $C(O)arC_{1-4}$ alkyl, - $C(O)$ -heteroaryl, - $C(OO)$ -cycloalkyl and - $C(O)O-C_{1-4}$ alkyl;
 wherein the C_{1-4} alkyl, aryl, ar C_{1-4} alkyl, partially unsaturated carbocyclyl, heteroaryl, heterocycloalkyl or cycloalkyl group, whether alone or part of a substituent group, is optionally substituted with one to three substituents independently selected from halogen, hydroxy, carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, $N(R^E)_2$, $N(R^E)_2-C_{1-4}$ alkyl, $(CH_3)_3CO-C(O)-N(R^E)-C_{1-4}$ alkyl, nitro, trifluoromethyl, trifluoromethoxy, phenyl, phenoxy, heteroaryl, cycloalkyl, 1-phenyl-pyrazol-2-yl-aminosulfonyl or C_{1-4} alkylthio;

alternatively when R^1 and R^2 are both bound to the same nitrogen atom, R^1 and R^2 are taken together with the nitrogen atom to which they are bound to form a group selected from heterocycloalkyl and heteroaryl;
 wherein the heteroaryl or heterocycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, carboxy, C_{1-4} alkyl, hydroxy substituted C_{1-4} alkyl, C_{1-4} alkoxy, phenyl, ar C_{1-4} alkyl, heterocycloalkyl, C_{1-4} alkoxycarbonyl, amino, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, di(C_{1-4} alkyl)amino-carbonyl, t-butoxycarbonylamino or phenylamino- C_{1-4} alkyl;
 wherein the phenyl or ar C_{1-4} alkyl substituent is optionally substituted with one or two substituents independently selected from chloro, trifluoromethyl or chlorophenyl;

R^3 is aryl; wherein the aryl group is optionally substituted with one or more substituents independently selected from halogen;

n is 0;

L^1 is C_{1-4} alkyl;

R^5 is selected from the group consisting of halogen, C_{1-4} alkyl and trifluoromethyl;

R^6 is $-(L^2)_0-R^7$;

5 R^7 is selected from the group consisting of aryl and heteroaryl; or a pharmaceutically acceptable salt thereof.

4. A compound as in Claim 3 wherein

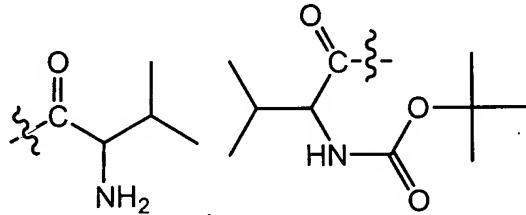
R^0 is selected from the group consisting of $-CH_2-CH(OH)-CH_2-X$ and –

10 $CH_2-CH_2-CH(OH)-CH_2-X$;

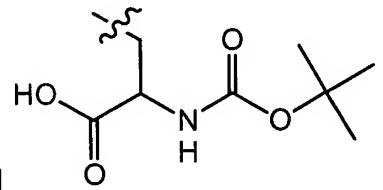
X is selected from the group consisting of $-NR^1R^2$, $-OR^1$, $-SR^1$, $-S-$

$CH_2CH(CO_2H)-NH-C(O)-CH_3$ and $-S-CH_2CH(CO_2H)-NH-C(O)O)C(CH_3)_3$;

R^1 is selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, n-butyl, t-butyl, amino-n-propyl, dimethylaminoethyl, benzyl,



15 phenylethyl, 4-methyl-benzyl, , 2-(3,4-dimethoxy-phenyl)ethyl, 3-methyl-phenyl, ethoxy-carbonyl-methyl, 2-amino-2-

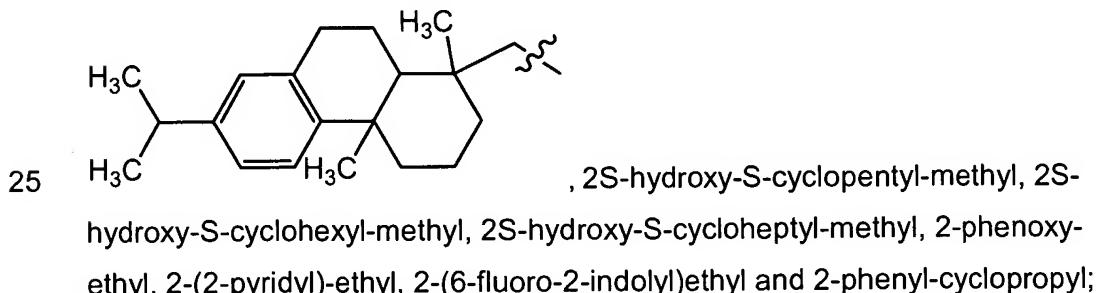
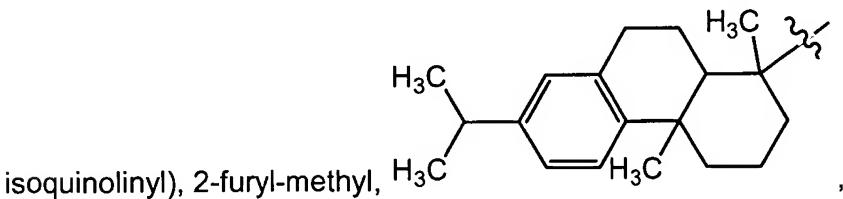


methoxycarbonyl-ethyl, t-butoxycarbonyl and ;

R^2 is selected from the group consisting of hydrogen, methyl, methoxy, ethyl, carboxy-methyl, ethoxycarbonylmethyl, 2,2,2,-triuoroethyl, ethoxy,

20 dimethylaminoethyl, t-butoxycarbonylamino-ethyl, n-butyl, t-butyl, n-propyl, 3-hydroxy-n-propyl, 3-methoxy-n-propyl, methylamino-n-propyl, dimethylamino-n-propyl, di(n-butyl)amino-n-propyl, t-butoxycarbonylamino-n-propyl, 3-phenyl-n-propyl, 3-(2-pyridyl)-n-propyl, t-butoxycarbonyl, cyclopropyl, phenyl, 4-fluorophenyl, 4-methylphenyl, 3,4-dimethoxyphenyl, 2-aminophenyl, 4-biphenyl, 25 2-ethoxyphenyl, 4-((1-phenyl-pyrazol-2-yl)-aminosulfonyl)-phenyl, 4-cyclohexylphenyl, 4-(aminoethyl)phenyl, 4-(t-butoxycarbonylamino-ethyl)-

phenyl, -CH(CH₃)-phenyl, benzyl, benzyloxy, 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl, 2-methoxybenzyl, 3-methoxybenzyl, 4-methoxybenzyl, 2-ethoxybenzyl, 3-ethoxybenzyl, 2-bromobenzyl, 3-bromobenzyl, 4-bromobenzyl, 3-chlorobenzyl, 4-chlorobenzyl), 3-iodobenzyl, 2-fluorobenzyl, 3-fluorobenzyl,
5 4-fluorobenzyl, 2-trifluoromethylbenzyl, 3-trifluoromethylbenzyl, 4-trifluoromethylbenzyl, 4-trifluoromethoxybenzyl, 4-methoxycarbonylbenzyl, 2,3-dimethoxybenzyl, 2,4-dichlorobenzyl, 3,4-dichlorobenzyl, 2,4-difluorobenzyl, 2,5-difluorobenzyl, 3,4-difluorobenzyl, 3,4,5-trimethoxybenzyl, 2,4,6-trimethoxybenzyl, 4-carboxybenzyl, 3-nitrobenzyl, 4-nitrobenzyl, 2,4-dimethoxybenzyl, 3,4-dimethoxybenzyl, 3,5-dimethoxybenzyl, 3,4-difluorobenzyl, 3,5-di(trifluoromethyl)benzyl, 4-(dimethylamino)benzyl, 2-phenylethyl, 2-(4-bromophenyl)ethyl, 2-(3-methoxyphenyl)ethyl, 2-(4-methoxyphenyl)ethyl, 2-(3,4-dimethoxyphenyl)ethyl, 2-(2-nitro-4,5-dimethoxy-phenyl)ethyl, 3-(4-morpholiny)-n-propyl, 2-(4-morpholiny)ethyl, 2-(4-imidazolyl)ethyl, 1-adamantanyl, 1-adamantanyl-methyl, (2,5-dimethoxy-2,5-dihydro-fur-2-yl)methyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyridyl-methyl, 3-pyridyl-methyl, 4-pyridyl-methyl, 2-(3,4-dimethyl-pyridyl), 2-(5-bromopyridyl), 2-(4,6-dimethyl-pyridyl), 2-(5-methyl-pyridyl), 3-(6-methoxy-pyridyl), 6-methylthio-2-pyridyl-carbonyl, thienyl-methyl, 2-thienylethyl, 4-pyridinyl, 1-naphthyl, 1-naphthyl-methyl, 1-(3,4-methylenedioxypyphenyl)methyl, 2-(3,4-methylenedioxypyphenyl)ethyl, 1-phenyl-2-(t-butoxycarbonyl)ethyl, -C(O)-C(OCH₃)(CF₃)-phenyl, -C(O)O-(2-isopropyl-5-methyl-cyclohexyl), 1-(4-ethoxycarbonyl-piperidinyl), 2-(3H-imidazol4-yl)ethyl, 2-(1,2,3,4-tetrahydro-



alternatively when R^1 and R^2 are both bound to the same nitrogen atom, R^1 and R^2 are taken together with the nitrogen atom to which they are bound to form a group selected from 1-morpholinyl, 1-(4-(3-trifluoromethyl-phenyl)-piperazinyl), 1-(4-piperidinyl-piperidinyl), 1-(4-pyrrolidinyl-piperidinyl), 1-(4-phenyl-piperidinyl), 1-(3-hydroxy-piperidinyl), 1-(4-hydroxy-piperidinyl), 1-(3-hydroxymethyl-piperidinyl), 1-(3,5-dimethyl-piperidinyl), 1-(4-dimethylamino-piperidinyl), 1-(4-(3,4-methylenedioxyphenylmethyl)-piperazinyl), 1-(3-diethylaminocarbonyl)-piperidinyl), 1-(4-t-butoxycarbonylamino-piperidinyl), 1-(2,3-dihydro-1H-pyrrolyl), 1-(4-[(4-chlorophenyl)-phenyl-methyl]-piperazinyl), 2-(1,2,3,4-tetrahydro-isoquinoliny), 1-(4-t-butoxycarbonyl-piperazinyl), 2-(1,2,3,4-tetrahydro-6,7-dimethoxy-isoquinoliny), 4-(2,6-dimethyl-morpholinyl), 1-(4-benzyl-piperazinyl), 1-pyrrolidinyl, 1-(2,3-dihydro-pyrrolidinyl), 1-(3-hydroxy-pyrrolidinyl), 1-(3-(S)-hydroxy-pyrrolidinyl), 1-piperidinyl, 1-(3-ethoxycarbonyl-piperidinyl), 1-(4-ethoxycarbonyl-piperidinyl), 1-imidazolyl, 1-(2-(phenylamino-methyl)-N-pyrrolidinyl), 1-(3-(R)-dimethylamino-pyrrolidinyl), 1-(3-(R)-hydroxy-pyrrolidinyl), 1-(3,4-dihydroxy-2,5-bis-hydroxymethyl-pyrrolidinyl), 1-(3-(R)-t-butoxycarbonylamino-pyrrolidinyl), 1-(3-(S)-ethylamino-pyrrolidinyl), 1-(3-(R)-amino-pyrrolidinyl), 1-(3-(S)-amino-pyrrolidinyl), 1-(3-(R)-methylamino-pyrrolidinyl), 1-(3-(S)-methylamino-pyrrolidinyl), 1-(3-(N-methyl-N-t-butoxycarbonyl-amino)-pyrrolidinyl) or 1-(2-(3,5-dichlorophenyl)-3-methyl-5-carboxy-1,2,4-triazolyl);

R^3 is selected from the group consisting of phenyl and 4-fluorophenyl;

L^1 is selected from the group consisting of $-CH_2-$, $-CH(CH_3)-$ and $-$

25 CH_2CH_2- :



is selected from the group consisting of cyclooctyl, 1-acenaphthenyl, R-1-acenaphthenyl, S-1-acenaphthenyl, cyclohexyl, phenyl, 1-naphthyl, 2-naphthyl, 1,2,3,4-tetrahydro-naphthyl, 2-thienyl, benzothienyl, 4,5,6,7-tetrahydro-benzothienyl, bicyclo[3.1.1]hepten-2-yl, bicyclo[3.1.1]heptyl and (3aS)-2,3,3a,4,5,6-hexahydro-1H-phenalen-1-yl;

R^5 is selected from the group consisting of chloro, methyl, n-propyl and trifluoromethyl;

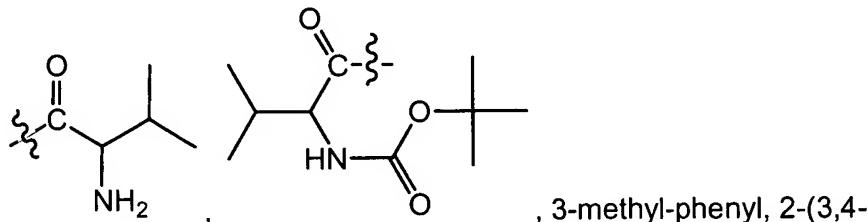
R^7 is selected from the group consisting of phenyl and 2-thienyl; or a pharmaceutically acceptable salt thereof.

5

5. A compound as in Claim 4 wherein

X is selected from the group consisting of $-NR^1R^2$, $-SR^1$ and $-S-CH_2CH(CO_2H)-NH-C(O)-CH_3$.

R^1 is selected from the group consisting of hydrogen, methyl, ethyl, n-
10 propyl, n-butyl, t-butyl, dimethylaminoethyl, benzyl, phenylethyl,



, 3-methyl-phenyl, 2-(3,4-

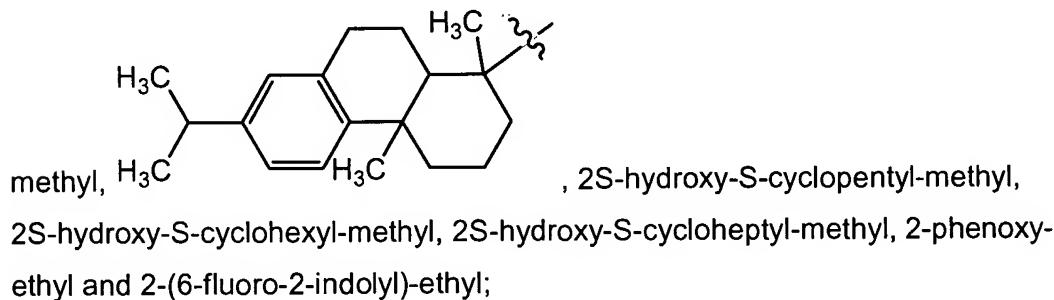
dimethoxyphenyl)-ethyl, ethoxycarbonyl-methyl, dimethylamino-ethyl and 2-amino-2-methoxycarbonyl-ethyl;

R^2 is selected from the group consisting of hydrogen, methyl, methoxy, ethyl, ethoxycarbonyl-methyl, 2,2,2-trifluoroethyl, ethoxy, dimethylaminoethyl, n-butyl, t-butyl, n-propyl, di(n-butyl)amino-n-propyl, 3-phenyl-n-propyl, 3-(2-pyridyl)-n-propyl, cyclopropyl, phenyl, 4-fluorophenyl, 4-methylphenyl, 2-aminophenyl, 4-(t-butoxycarbonylamino-ethyl)-phenyl, 3,4-dimethoxyphenyl, 4-biphenyl, 2-ethoxyphenyl, 4-((1-phenyl-pyrazol-2-yl)-aminosulfonyl)-phenyl, 4-(aminoethyl)-phenyl, benzyl, benzyloxy, 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl, 2-methoxybenzyl, 3-methoxybenzyl, 4-methoxybenzyl, 2-ethoxybenzyl, 3-ethoxybenzyl, 2-bromobenzyl, 3-bromobenzyl, 4-bromobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 3-iodobenzyl, 2-fluorobenzyl, 3-fluorobenzyl, 4-fluorobenzyl, 2-trifluoromethylbenzyl, 3-trifluoromethylbenzyl, 4-trifluoromethylbenzyl, 4-trifluoromethoxybenzyl, 4-methoxycarbonyl-benzyl, 2,3-dimethoxybenzyl, 2,4-dichlorobenzyl, 3,4-dichlorobenzyl, 2,4-difluorobenzyl, 2,5-difluorobenzyl, 3,4-difluorobenzyl, 3,4,5-trimethoxybenzyl, 2,4,6-trimethoxybenzyl, 4-carboxybenzyl, 3-nitrobenzyl, 4-nitrobenzyl, 2,4-dimethoxybenzyl, 3,4-dimethoxybenzyl, 3,5-dimethoxybenzyl, 3,4-

difluorobenzyl, 3,5-di(trifluoromethyl)-benzyl, 2-phenylethyl, 2-(4-bromophenyl)ethyl, 2-(3-methoxyphenyl)ethyl, 2-(4-methoxyphenyl)ethyl, 2-(3,4-dimethoxyphenyl)ethyl, 2-(2-nitro-4,5-dimethoxy-phenyl)ethyl, 3-(4-morpholinyl)-n-propyl, 2-(4-morpholinyl)ethyl, 2-(4-imidazolyl)ethyl,

5 adamantanyl, 1-adamantanyl-methyl, 2-(2,5-dimethoxy-2,5-dihydro-furyl)methyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyridyl-methyl, 3-pyridyl-methyl, 4-pyridyl-methyl, 2-(3,4-dimethyl-pyridyl), 2-(5-bromopyridyl), 2-(4,6-dimethyl-pyridyl), 2-(5-methyl-pyridyl), 3-(6-methoxy-pyridyl), thienylmethyl, 2-thienylethyl, 1-naphthyl, 1-naphthyl-methyl, 1-(3,4-

10 methylenedioxyphenyl)methyl, 2-(3,4-methylenedioxyphenyl)ethyl, 2-furyl-



15 alternatively when R¹ and R² are both bound to the same nitrogen atom, R¹ and R² are taken together with the nitrogen atom to which they are bound to form a group selected from 1-(4-(3-trifluoromethyl-phenyl)-piperazinyl), 1-(4-phenyl-piperidinyl), 1-(4-piperidinyl-piperidinyl), 1-(4-(3,4-methylenedioxyphenyl-methyl)-piperazinyl), 1-(3-(diethylaminocarbonyl)-piperidinyl), 1-(4-[(4-chlorophenyl)-phenylmethyl]-piperazinyl), 2-(1,2,3,4-tetrahydro-isoquinolinyl), 1-(4-t-butoxycarbonyl-piperazinyl), 2-(1,2,3,4-tetrahydro-6,7-dimethoxy-isoquinolinyl), 4-(2,6-dimethyl-morpholinyl), 1-(4-benzyl-piperazinyl), 1-morpholinyl, 1-pyrrolidinyl, 1-(2,3-dihydro-pyrrolidinyl), 1-piperidinyl, 1-(3,5-dimethyl-piperidinyl), 1-(3-hydroxymethyl-piperidinyl), 1-(3-ethoxycarbonyl-piperidinyl), 1-(4-(ethoxycarbonyl)-piperidinyl), 1-imidazolyl and 1-(2-(phenylamino-methyl)-N-pyrrolidinyl);

20

25

L¹ is selected from the group consisting of -CH₂- and -CH₂-CH₂-;



is selected from the group consisting of cyclooctyl, 1-acenaphthenyl, R-1-acenaphthenyl, S-1-acenaphthenyl, cyclohexyl, phenyl, 1-naphthyl and (3a-S)-2,3,3a,4,5,6-hexahydro-1H-phenalen-2-yl;

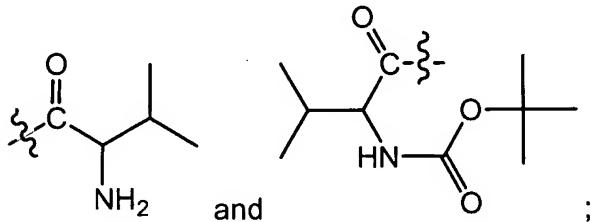
p is an integer from 0 to 2;

5 R⁷ is 2-thienyl;

or a pharmaceutically acceptable salt thereof.

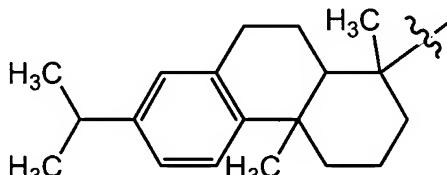
6. A compound as in Claim 5 wherein

10 R¹ is selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, n-butyl, t-butyl, dimethylaminoethyl, benzyl, phenylethyl, 2-(3,4-dimethoxyphenyl)-ethyl, dimethylamino-ethyl, ethoxycarbonyl-methyl,



15 R² is selected from the group consisting of hydrogen, methyl, methoxy, ethyl, ethoxycarbonyl-methyl, ethoxy, dimethylaminoethyl, n-butyl, n-propyl, di(n-butyl)amino-n-propyl, 3-phenyl-n-propyl, 3-(2-pyridyl)-n-propyl, cyclopropyl, phenyl, 4-fluorophenyl, 4-methylphenyl, 2-aminophenyl, 3,4-dimethoxyphenyl, 4-(t-butoxycarbonylamino-ethyl)-phenyl, 4-biphenyl, 2-ethoxyphenyl, 4-((1-phenyl-pyrazol-2-yl)-aminosulfonyl)-phenyl, 4-(aminoethyl)-phenyl, benzyl, benzyloxy, 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl, 2-methoxybenzyl, 20 3-methoxybenzyl, 4-methoxybenzyl, 2-ethoxybenzyl, 3-ethoxybenzyl, 2-bromobenzyl, 3-bromobenzyl, 4-bromobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 3-iodobenzyl, 2-fluorobenzyl, 3-fluorobenzyl, 4-fluorobenzyl, 2-trifluoromethylbenzyl, 3-trifluoromethylbenzyl, 4-trifluoromethylbenzyl, 4-trifluoromethoxybenzyl, 4-methoxycarbonyl-benzyl, 2,3-dimethoxybenzyl, 2,4-dichlorobenzyl, 3,4-dichlorobenzyl, 2,4-difluorobenzyl, 2,5-difluorobenzyl, 3,4,5-trimethoxybenzyl, 2,4,6-trimethoxybenzyl, 3-nitrobenzyl, 4-nitrobenzyl, 2,4-dimethoxybenzyl, 3,4-dimethoxybenzyl, 3,5-dimethoxybenzyl, 3,4-difluorobenzyl, 3,5-di(trifluoromethyl)-benzyl, 2-phenylethyl, 2-(4-

bromophenyl)ethyl, 2-(3-methoxyphenyl)ethyl, 2-(4-methoxyphenyl)ethyl, 2-(3,4-dimethoxyphenyl)ethyl, 2-(2-nitro-4,5-dimethoxy-phenyl)ethyl, 3-(4-morpholinyl)-n-propyl, 2-(4-morpholinyl)ethyl, 2-(4-imidazolyl)ethyl, 1-adamantanyl, 1-adamantanyl-methyl, 2-(2,5-dimethoxy-2,5-dihydrofuryl)methyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyridyl-methyl, 3-pyridyl-methyl, 4-pyridyl-methyl, 2-(3,4-dimethyl-pyridyl), 2-(5-bromopyridyl), 2-(4,6-dimethyl-pyridyl), 2-(5-methyl-pyridyl), 3-(6-methoxy-pyridyl), thienylmethyl, 2-thienylethyl, 1-naphthyl, 1-naphthyl-methyl, 1-(3,4-methylenedioxyphenyl)methyl, 2-(3,4-methylenedioxyphenyl)ethyl, 2-furyl-methyl, 2S-hydroxy-S-cyclopentyl-methyl, 2S-hydroxy-S-cyclohexyl-methyl, 2S-hydroxy-S-cycloheptyl-methyl and 2-phenoxy-ethyl;



alternatively when R¹ and R² are both bound to the same nitrogen atom, 15 R¹ and R² are taken together with the nitrogen atom to which they are bound to form a group selected from 1-(4-(3-trifluoromethyl-phenyl)-piperazinyl), 1-(4-phenyl-piperidinyl), 1-(4-piperidinyl-piperidinyl), 1-(4-(3,4-methylenedioxyphenyl-methyl)-piperazinyl), 1-(3-(diethylaminocarbonyl)-piperidinyl), 1-(4-[(4-chlorophenyl)-phenylmethyl]-piperazinyl), 2-(1,2,3,4-tetrahydro-isoquinolinyl), 1-(4-t-butoxycarbonyl-piperazinyl), 2-(1,2,3,4-tetrahydro-6,7-dimethoxy-isoquinolinyl), 4-(2,6-dimethyl-morpholinyl), 1-(4-benzyl-piperazinyl), 1-(3,5-dimethyl-piperidinyl), 1-(3-hydroxymethyl-piperidinyl), 1-(3-ethoxycarbonyl-piperidinyl), 1-(4-(ethoxycarbonyl)-piperidinyl), 1-piperidinyl, 1-morpholinyl, 1-pyrrolidinyl, 1-imidazolyl, 1-(2,3-dihydro-25 pyrrolidinyl), and 1-(2-(phenylamino-methyl)-N-pyrrolidinyl);

p is an integer from 0 to 1;

R⁵ is selected from the group consisting of methyl, n-propyl and trifluoromethyl;

or a pharmaceutically acceptable salt thereof.

7. A compound as in Claim 4 wherein

R^0 is $-\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{X}$;

X is $-\text{NR}^1\text{R}^2$;

R^1 is selected from the group consisting of hydrogen, 2-(3,4-dimethoxyphenyl)-ethyl, 1-(3,4-dimethoxyphenyl)-n-ethyl and amino-n-propyl;

5 R^2 is selected from the group consisting of hydrogen, methyl, n-butyl, 3-hydroxy-n-propyl, 3-methoxy-n-propyl, methylamino-n-propyl, dimethylamino-n-propyl, t-butoxycarbonylamino-n-propyl, N-methyl-N-t-butoxycarbonyl-amino-n-ethyl, 3-nitrobenzyl, 4-methoxycarbonyl-benzyl, $-\text{CH}(\text{CH}_3)\text{-phenyl}$, 4-pyridinyl, 1-(4-ethoxycarbonyl-piperidinyl) and 2-(3H-imidazol-4-yl)-ethyl;

10 alternatively when R^1 and R^2 are both bound to the same nitrogen atom, R^1 and R^2 are taken together with the nitrogen atom to which they are bound to form a group selected from 2-(1,2,3,4-tetrahydro-6,7-dimethoxy-isoquinolinyl), 1-(4-[(4-chlorophenyl)-phenyl-methyl]-piperazinyl), 1-pyrrolidinyl, 1-(3-hydroxy-pyrrolidinyl), 1-(3-(S)-hydroxy-pyrrolidinyl), 1-(3-(R)-hydroxy-pyrrolidinyl), 1-(4-hydroxy-piperidinyl), 1-(3-(R)-dimethylamino-pyrrolidinyl), 1-(4-t-butoxycarbonylamino-pyrrolidinyl), 1-(3-(R)-t-butoxycarbonylamino-pyrrolidinyl), 1-(3-(R)-amino-pyrrolidinyl), 1-(3-(S)-amino-pyrrolidinyl), 1-(3-(R)-methylamino-pyrrolidinyl), 1-(3-(S)-methylamino-pyrrolidinyl), 1-(3-(S)-ethylamino-pyrrolidinyl), 1-(4-dimethylamino-pyrrolidinyl), 1-(3-(N-methyl-N-t-butoxycarbonyl-amino-pyrrolidinyl) or 1-(2-(3,5-dichlorophenyl)-3-methyl-5-carboxy-1,2,4-triazolyl);

15 R^3 is selected from the group consisting of phenyl and 4-fluorophenyl;

L^1 is selected from the group consisting of $-\text{CH}_2-$ and $-\text{CH}_2\text{CH}_2-$;

20  is selected from the group consisting of cyclooctyl, 1-naphthyl, 1-acenaphthenyl, R-1-acenaphthenyl, S-1-acenaphthenyl, bicyclo[3.1.1.]hepten-2-yl, bicyclo[3.1.1]heptyl and (3aS)-2,3,3a,4,5,6-hexahydro-1H-phenalen-1-yl.

25 p is an integer from 0 to 1;

R^5 is methyl;

30 q is 0;

or a pharmaceutically acceptable salt thereof.

8. A compound as in Claim 7 wherein

5 R^1 is selected from the group consisting of hydrogen, 1-(3,4-dimethoxyphenyl)-n-ethyl and amino-n-propyl;

10 R^2 is selected from the group consisting of hydrogen, methyl, n-butyl, 3-hydroxy-n-propyl, 3-methoxy-n-propyl, methylamino-n-propyl, dimethylamino-n-propyl, N-methyl-N-t-butoxycarbonyl-amino-n-ethyl, 3-nitrobenzyl, 4-methoxycarbonyl-benzyl, $-\text{CH}(\text{CH}_3)\text{-phenyl}$, 4-pyridinyl and 2-(3H-imidazol-4-yl)-ethyl;

15 alternatively when R^1 and R^2 are both bound to the same nitrogen atom, R^1 and R^2 are taken together with the nitrogen atom to which they are bound to form a group selected from 2-(1,2,3,4-tetrahydro-6,7-dimethoxy-isoquinolinyl), 1-(4-[(4-chlorophenyl)-phenyl-methyl]-piperazinyl), 1-pyrrolidinyl, 1-(3-hydroxy-pyrrolidinyl), 1-(3-(R)-hydroxy-pyrrolidinyl), 1-(4-hydroxy-piperidinyl), 1-(3-(R)-dimethylamino-pyrrolidinyl), 1-(4-t-butoxycarbonylamino-pyrrolidinyl), 1-(3-(R)-t-butoxycarbonylamino-pyrrolidinyl), 1-(3-(R)-amino-pyrrolidinyl), 1-(3-(S)-amino-pyrrolidinyl), 1-(3-(R)-methylamino-pyrrolidinyl), 1-(3-(S)-methyamino-pyrrolidinyl), 1-(3-(S)-ethylamino-pyrrolidinyl), 1-(4-dimethylamino-pyrrolidinyl), 1-(3-(N-methyl-N-t-butoxycarbonyl-amino-pyrrolidinyl) or 1-(2-(3,5-dichlorophenyl)-3-methyl-5-carboxy-1,2,4-triazolyl);



is selected from the group consisting cyclooctyl, 1-naphthyl, 1-acenaphthenyl, R-1-acenaphthenyl, S-1-acenaphthenyl, bicyclo[3.1.1.]hepten-2-yl, bicyclo[3.1.1]heptyl and (3aS)-2,3,3a,4,5,6-hexahydro-1H-phenalen-1-yl. or a pharmaceutically acceptable salt thereof.

25

9. A compound as in Claim 1 selected from the group consisting of

15 8-(R) acenaphthen-1-yl-3-(3-amino-2-(S)-hydroxy-propyl)-1-(4-fluoro-phenyl)-1,3,8-triaza-spiro[4.5]decan-4-one;

20 8-(R) acenaphthen-1-yl-3-(3-amino-2-(R)-hydroxy-propyl)-1-(4-fluoro-phenyl)-1,3,8-triaza-spiro[4.5]decan-4-one;

8-(R)-Acenaphthen-1-yl-3-(3-dimethylamino-2-(R)-hydroxy-propyl)-1-(4-fluoro-phenyl)-1,3,8-triaza-spiro[4.5]decan-4-one;

3-(3-Amino-2-(R)-hydroxy-propyl)-1-(4-fluoro-phenyl)-8-(8-methyl-naphthalen-1-ylmethyl)-1,3,8-triaza-spiro[4.5]decan-4-one;

5 3-(3-Dimethylamino-2-(R)-hydroxy-propyl)-1-(4-fluoro-phenyl)-8-(8-methyl-naphthalen-1-ylmethyl)-1,3,8-triaza-spiro[4.5]decan-4-one;

8-(R)-Acenaphthen-1-yl-1-(4-fluoro-phenyl)-3-[2-(R)-hydroxy-3-(3-hydroxymethyl-piperidin-1-yl)-propyl]-1,3,8-triaza-spiro[4.5]decan-4-one;

3-(3-Amino-2-(R)-hydroxy-propyl)-8-cyclooctyl-1-(4-fluoro-phenyl)-1,3,8-triaza-spiro[4.5]decan-4-one;

10 3-(3-Amino-2-(R)-hydroxy-propyl)-1-(4-fluoro-phenyl)-8-1-(S)-(3aS)-(2,3,3a,4,5,6-hexahydro-1H-phenalen-1-yl)-1,3,8-triaza-spiro[4.5]decan-4-one;

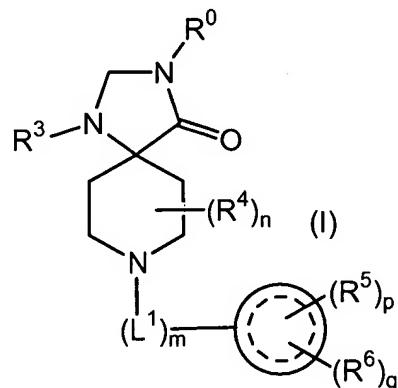
1-(4-Fluoro-phenyl)-3-[2-(R)-hydroxy-3-(3-hydroxy-propylamino)-propyl]-8-(8-methyl-naphthalen-1-ylmethyl)-1,3,8-triaza-spiro[4.5]decan-4-one;

15 1-(4-Fluoro-phenyl)-3-[2-(R)-hydroxy-3-(3-methylamino-propylamino)-propyl]-8-(8-methyl-naphthalen-1-ylmethyl)-1,3,8-triaza-spiro[4.5]decan-4-one;

3-[3-(3-Dimethylamino-propylamino)-2-(R)-hydroxy-propyl]-1-(4-fluoro-phenyl)-8-(8-methyl-naphthalen-1-ylmethyl)-1,3,8-triaza-spiro[4.5]decan-4-one
and pharmaceutically acceptable salts thereof.

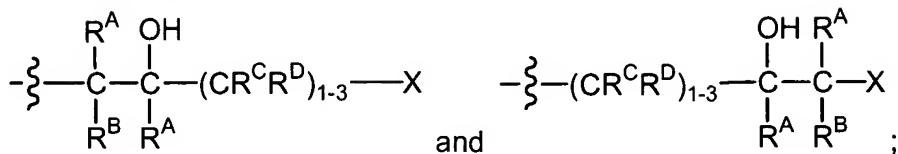
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10. A compound of the formula (I)



wherein

R^0 is selected from the group consisting of



each R^A and R^B is independently selected from the group consisting of hydrogen and C_{1-4} alkyl;

5 each R^C and R^D is independently selected from the group consisting of hydrogen, hydroxy, carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, nitro, cyano, $N(R^E)_2$, aryl, ar C_{1-4} alkyl, heteroaryl or heterocycloalkyl; wherein the aryl, ar C_{1-4} alkyl, heteroaryl or heterocycloalkyl substituent is optionally substituted with one or more substituents independently selected from hydroxy, carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, nitro, cyano or $N(R^E)_2$;

10 each R^E is independently selected from the group consisting of hydrogen and C_{1-4} alkyl;

X is selected from the group consisting of $-NR^1R^2$, $-C(O)-NR^1R^2$, $-NR^1-C(O)-R^2$, $-OR^1$, $-SR^1$, $-SOR^1$, $-SO_2R^1$, $-S-(C_{2-4}\text{alkyl})-NR^1R^2$, $-S-(C_{2-4}\text{alkyl})-C(O)O-C(CH_3)_3$, $-SO-(C_{1-4}\text{alkyl})-NR^1R^2$ and $-SO_2-(C_{1-4}\text{alkyl})-NR^1R^2$; wherein the alkyl portion of the $-S-(C_{2-4}\text{alkyl})-NR^1R^2$, $-SO-(C_{1-4}\text{alkyl})-NR^1R^2$ or $-SO_2-(C_{1-4}\text{alkyl})-NR^1R^2$ group is optionally substituted with one or more substituents independently selected from carboxy, hydroxy, hydroxy C_{1-4} alkyl, C_{1-4} alkyl, C_{1-4} alkoxycarbonyl or $-CONR^1R^2$;

15 20 each R^1 and R^2 is independently selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{1-8} alkoxy, cycloalkyl, cycloalkyl- C_{1-4} alkyl, partially unsaturated carbocyclicl, aryl, ar C_{1-4} alkyl, ar C_{1-4} alkoxy, heteroaryl, heteroaryl- C_{1-4} alkyl, heterocycloalkyl, heterocycloalkyl- C_{1-4} alkyl, $-C(O)-C_{1-6}$ alkyl, $-C(O)-aryl$, $-C(O)-arC_{1-4}$ alkyl, $-C(O)-heteroaryl$ and $-C(O)-heterocycloalkyl$; wherein the C_{1-8} alkyl, cycloalkyl, partially unsaturated carbocyclicl, aryl, ar C_{1-8} alkyl, heteroaryl or heterocycloalkyl group, whether alone or part of a substituent group, is optionally substituted with one or more substituents independently selected from halogen, hydroxy, carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano, $-C(O)-C_{1-4}$ alkyl, C_{1-4} alkoxycarbonyl, $N(R^E)_2$,

25 30 $N(R^E)_2-C_{1-4}$ alkyl, $N(R^E)-C(O)C(CH_3)_3$, aryl, aryloxy, cycloalkyl, heteroaryl, aryl substituted heteroarylaminosulfonyl or C_{1-6} alkylthio;

alternatively when R^1 and R^2 are both bound to the same nitrogen atom, R^1 and R^2 are taken together with the nitrogen atom to which they are bound to form a heteroaryl or heterocycloalkyl group; wherein the heteroaryl or heterocycloalkyl group is optionally substituted with one or more substituents

5 independently selected from halogen, hydroxy, carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, trifluoromethyl, trifluoromethoxy, nitro, cyano, $N(R^E)_2$, aryl, ar C_{1-4} alkyl, heteroaryl, heterocycloalkyl, di(C_{1-6})alkylamino-carbonyl, t-butoxycarbonyl or arylamino- C_{1-4} alkyl; wherein the aryl, ar C_{1-4} alkyl, heteroaryl or heterocycloalkyl substituent is optionally further substituted with one or more

10 substituents independently selected from halogen, hydroxy, carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano, $N(R^E)_2$ or substituted phenyl; wherein the substituents on the phenyl are one or more independently selected from halogen, hydroxy, carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano or $N(R^E)_2$;

15 R^3 is selected from the group consisting of aryl, ar C_{1-6} alkyl and heteroaryl; wherein the aryl, ar C_{1-6} alkyl or heteroaryl group is optionally substituted with one or more substituents independently selected from halogen, hydroxy, carboxy, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano or $N(R^E)_2$;

20 n is an integer from 0 to 2;
 R^4 is selected from the group consisting of hydroxy, C_{1-4} alkyl and hydroxy substituted C_{1-4} alkyl;
 m is an integer from 0 to 1;
 L^1 is selected from the group consisting of C_{1-6} alkyl and C_{3-6} alkenyl;

25 wherein the double bond of the C_{3-6} alkenyl group is at least one carbon atom removed from the attachment point to the N atom; and wherein the C_{1-6} alkyl or C_{3-6} alkenyl group is optionally substituted with one to two substituents independently selected from hydroxy, fluoro, C_{1-6} alkyl, fluorinated C_{1-6} alkyl or C_{1-6} alkoxy;

30  is selected from the group consisting of cycloalkyl, partially unsaturated carbocyclyl, aryl, heteroaryl and heterocycloalkyl;

p is an integer from 0 to 5;

R^5 is selected from the group consisting of hydroxy, carboxy, halogen, C_{1-6} alkyl, C_{1-6} alkoxy, nitro, cyano, NR^1R^2 , trifluoromethyl, trifluoromethoxy; C_{1-4} alkoxycarbonyl, $-SO-NR^1R^2$, $-SO_2-NR^1R^2$ and $-C(O)-NR^1R^2$;

5 q is an integer from 0 to 1;

R^6 is selected from the group consisting of $-(L^2)_{0-1}R^7$;

L^2 is selected from the group consisting of $-C_{1-6}$ alkyl-, $-C_{2-4}$ alkenyl-, $-C_{2-6}$ alkynyl-, $-O-$, $-S-$, $-NH-$, $-N(C_{1-4}alkyl)-$, $-C_{1-6}$ alkyl-O-, $-C_{1-6}$ alkyl-S-, $-O-C_{1-6}$ alkyl-, $-S-C_{1-6}$ alkyl-, $-O-C_{2-6}$ alkyl-O-, $-S-C_{2-6}$ alkyl-S-, $-SO_2-$, $-SO_2NH-$, $-SO_2N(C_{1-4}alkyl)-$,

10 $-NH-SO_2-$, $-N(C_{1-4}alkyl)-SO_2-$, $-C(O)-O-$ and $-O-C(O)-$;

R^7 is selected from the group consisting of aryl, partially unsaturated carbocyclyl, cycloalkyl, heteroaryl and heterocycloalkyl; wherein the aryl, partially unsaturated carbocyclyl, cycloalkyl, heteroaryl or heterocycloalkyl group is optionally substituted with one or more substituents independently selected from hydroxy, carboxy, halogen, C_{1-6} alkyl, C_{1-6} alkoxy, nitro, cyano, $N(R^E)_2$, trifluoromethyl, trifluoromethoxy, C_{1-4} alkoxycarbonyl, $-SO_2-N(R^E)_2$ and $-C(O)-N(R^E)_2$;

or a pharmaceutically acceptable salt thereof.

20 11. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of Claim 1.

12. A pharmaceutical composition made by mixing a compound of Claim 1 and a pharmaceutically acceptable carrier.

25 13. A process for making a pharmaceutical composition comprising mixing a compound of Claim 1 and a pharmaceutically acceptable carrier.

14. A method of treating a disorder mediated by the ORL-1 receptor, in a subject in need thereof comprising administering to the subject a therapeutically effective amount of the compound of Claim 1.

15. The method of Claim 14, wherein the disorder mediated by the ORL-1 receptor is selected from the group consisting of anxiety, depression, panic, mania, dementia, bipolar disorder, substance abuse, neuropathic pain, acute pain, chronic pain, migraine, asthma, cough, psychosis, schizophrenia, epilepsy, hypertension, obesity, eating disorders, cravings, diabetes, cardiac arrhythmia, irritable bowel syndrome, Crohn's disease, urinary incontinence, adrenal disorders, attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), Alzheimer's disease, improved cognition, improved memory and mood stabilization.

10

16. A method of treating a disorder mediated by the ORL-1 receptor, in a subject in need thereof comprising administering to the subject a therapeutically effective amount of the composition of Claim 11.

15

17. A method of treating a condition selected from the group consisting of anxiety, depression, panic, mania, dementia, bipolar disorder, substance abuse, neuropathic pain, acute pain, chronic pain, migraine, asthma, cough, psychosis, schizophrenia, epilepsy, hypertension, obesity, eating disorders, cravings, diabetes, cardiac arrhythmia, irritable bowel syndrome, Crohn's disease, urinary incontinence, adrenal disorders, attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), Alzheimer's disease, improved cognition, improved memory and mood stabilization, in a subject in need thereof comprising administering to the subject a therapeutically effective amount of the compound of Claim 1.

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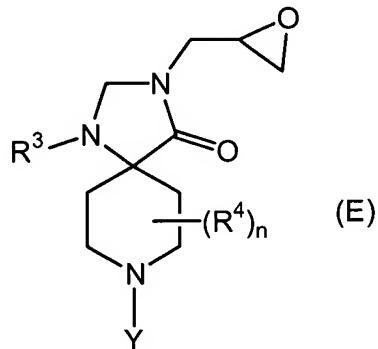
18. A method of treating a condition selected from the group consisting of anxiety, depression, panic, mania, dementia, bipolar disorder, substance abuse, neuropathic pain, acute pain, chronic pain, migraine, asthma, cough, psychosis, schizophrenia, epilepsy, hypertension, obesity, eating disorders, cravings, diabetes, cardiac arrhythmia, irritable bowel syndrome, Crohn's disease, urinary incontinence, adrenal disorders, attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), Alzheimer's disease, improved cognition, improved memory and mood stabilization, in a subject in

need thereof comprising administering to the subject a therapeutically effective amount of the composition of Claim 7.

19. The use of a compound as in Claim 1 for the preparation of a
 5 medicament for the treatment of (a) anxiety, (b) depression, (c) panic, (d) mania, (e) dementia, (f) bipolar disorder, (g) substance abuse, (h) neuropathic pain, (i) acute pain, (j) chronic pain, (k) migraine, (l) asthma, (m) cough, (n) psychosis, (o) schizophrenia, (p) epilepsy, (q) hypertension, (r) obesity, (s) eating disorders, (t) cravings, (u) diabetes, (v) cardiac arrhythmia, (w) irritable
 10 bowel syndrome, (x) Crohn's disease, (y) urinary incontinence, (z) adrenal disorders, (aa) attention deficit disorder (ADD), (bb) attention deficit hyperactivity disorder (ADHD), (cc) Alzheimer's disease, for (dd) improved cognition, (ee) improved memory or (ff) mood stabilization, in a subject in need thereof.

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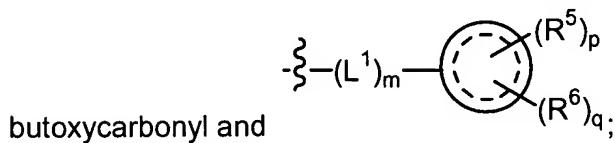
20. A compound of the formula (E)



wherein

R^3 is selected from the group consisting of aryl, arC₁₋₆alkyl and
 20 heteroaryl; wherein the aryl, arC₁₋₆alkyl or heteroaryl group is optionally substituted with one or more substituents independently selected from halogen, hydroxy, carboxy, C₁₋₄alkyl, C₁₋₄alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano or N(R^E)₂;
 each R^E is independently selected from hydrogen or C₁₋₄alkyl;
 25 n is an integer from 0 to 2;
 R^4 is selected from the group consisting of hydroxy, C₁₋₄alkyl and hydroxy substituted C₁₋₄alkyl;

Y is selected from the group consisting of hydrogen, C₁₋₄alkyl, t-



m is an integer from 0 to 1;

L¹ is selected from the group consisting of C₁₋₆alkyl and C₃₋₆alkenyl;

5 wherein the double bond of the C₃₋₆alkenyl group is at least one carbon atom removed from the attachment point to the N atom; and wherein the C₁₋₆alkyl or C₃₋₆alkenyl group is optionally substituted with one to two substituents independently selected from hydroxy, fluoro, C₁₋₆alkyl, fluorinated C₁₋₆alkyl or C₁₋₆alkoxy;

10  is selected from the group consisting of cycloalkyl, partially unsaturated carbocyclyl, aryl, heteroaryl and heterocycloalkyl;

p is an integer from 0 to 5;

R⁵ is selected from the group consisting of hydroxy, carboxy, halogen, C₁₋₆alkyl, hydroxy substituted C₁₋₆alkyl, C₁₋₆alkoxy, nitro, cyano, NR¹R²,

15 trifluoromethyl, trifluoromethoxy, C₁₋₄alkoxycarbonyl, -SO-NR¹R², -SO₂-NR¹R² and -C(O)-NR¹R²;

q is an integer from 0 to 1;

R⁶ is selected from the group consisting of -(L²)₀₋₁-R⁷;

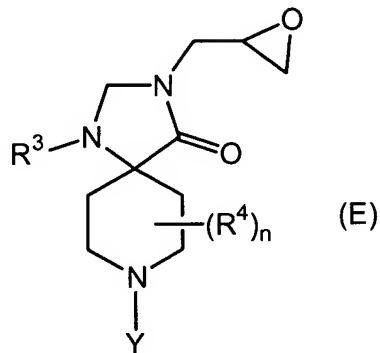
L² is selected from the group consisting of -C₁₋₆alkyl-, -C₂₋₄alkenyl-, -C₂₋₆alkynyl-, -O-, -S-, -NH-, -N(C₁₋₄alkyl)-, -C₁₋₆alkyl-O-, -C₁₋₆alkyl-S-, -O-C₁₋₆alkyl-, -S-C₁₋₆alkyl-, -O-C₂₋₆alkyl-O-, -S-C₂₋₆alkyl-S-, -SO₂-, -SO₂NH-, -SO₂N(C₁₋₄alkyl)-, -NH-SO₂-, -N(C₁₋₄alkyl)-SO₂-, -C(O)-O- and -O-C(O)-;

20 R⁷ is selected from the group consisting of aryl, partially unsaturated carbocyclyl, cycloalkyl, heteroaryl and heterocycloalkyl; wherein the aryl, partially unsaturated carbocyclyl, cycloalkyl, heteroaryl or heterocycloalkyl group is optionally substituted with one or more substituents independently selected from hydroxy, carboxy, halogen, C₁₋₆alkyl, C₁₋₆alkoxy, nitro, cyano, N(R^E)₂, trifluoromethyl, trifluoromethoxy, C₁₋₄alkoxycarbonyl, -SO₂-N(R^E)₂ and -C(O)-N(R^E)₂;

25

or a pharmaceutically acceptable salt thereof.

21. A compound of the formula (E)



5 wherein

R^3 is selected from the group consisting of aryl, arC₁₋₆alkyl and heteroaryl; wherein the aryl, arC₁₋₆alkyl or heteroaryl group is optionally substituted with one or more substituents independently selected from halogen, hydroxy, carboxy, C₁₋₄alkyl, C₁₋₄alkoxy, trifluoromethyl,

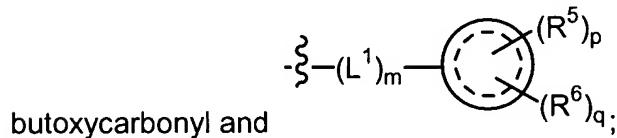
10 trifluoromethoxy, nitro, cyano or N(R^E)₂;

each R^E is independently selected from hydrogen or C₁₋₄alkyl;

n is an integer from 0 to 2;

R^4 is selected from the group consisting of hydroxy, C₁₋₄alkyl and hydroxy substituted C₁₋₄alkyl;

15 Y is selected from the group consisting of hydrogen, C₁₋₄alkyl, t-



butoxycarbonyl and

m is an integer from 0 to 1;

L^1 is selected from the group consisting of C₁₋₆alkyl and C₃₋₆alkenyl; wherein the double bond of the C₃₋₆alkenyl group is at least one carbon atom

20 removed from the attachment point to the N atom; and wherein the C₁₋₆alkyl or C₃₋₆alkenyl group is optionally substituted with one to two substituents independently selected from hydroxy, fluoro, C₁₋₆alkyl, fluorinated C₁₋₆alkyl or C₁₋₆alkoxy;



is selected from the group consisting of cycloalkyl, partially unsaturated carbocyclyl, aryl, heteroaryl and heterocycloalkyl;

p is an integer from 0 to 5;

R⁵ is selected from the group consisting of hydroxy, carboxy, halogen,

5 C₁₋₆alkyl, C₁₋₆alkoxy, nitro, cyano, NR¹R², trifluoromethyl, trifluoromethoxy, C₁₋₄alkoxycarbonyl, -SO-NR¹R², -SO₂-NR¹R² and -C(O)-NR¹R²;

q is an integer from 0 to 1;

R⁶ is selected from the group consisting of -(L²)₀₋₁-R⁷;

L² is selected from the group consisting of -C₁₋₆alkyl-, -C₂₋₄alkenyl-, -C₂₋₆alkynyl-, -O-, -S-, -NH-, -N(C₁₋₄alkyl)-, -C₁₋₆alkyl-O-, -C₁₋₆alkyl-S-, -O-C₁₋₆alkyl-, -S-C₁₋₆alkyl-, -O-C₂₋₆alkyl-O-, -S-C₂₋₆alkyl-S-, -SO₂-, -SO₂NH-, -SO₂N(C₁₋₄alkyl)-, -NH-SO₂-, -N(C₁₋₄alkyl)-SO₂-, -C(O)-O- and -O-C(O)-;

R⁷ is selected from the group consisting of aryl, partially unsaturated carbocyclyl, cycloalkyl, heteroaryl and heterocycloalkyl; wherein the aryl, partially unsaturated carbocyclyl, cycloalkyl, heteroaryl or heterocycloalkyl group is optionally substituted with one or more substituents independently selected from hydroxy, carboxy, halogen, C₁₋₆alkyl, C₁₋₆alkoxy, nitro, cyano, N(R^E)₂, trifluoromethyl, trifluoromethoxy, C₁₋₄alkoxycarbonyl, -SO₂-N(R^E)₂ and -C(O)-N(R^E)₂;

10 20 or a pharmaceutically acceptable salt thereof.